510(k) Summary

Afinion™ HbA1c, Afinion™ HbA1c Control &

Afinion™ AS100 Analyzer

1. Introduction

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for determination of substantial equivalence.

2. Submitter

Manufacturer/Owner
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Date prepared: March 3rd 2005

3. Device name

Trade name: Afinion™ HbA1c
Common name: Glycated Hemoglobin Assay
Classification name: Glycosylated Hemoglobin assay
Regulation Number: 21 CFR § 864.7470

4. Predicate Device

Predicate device name: DCA2000® Hemoglobin A1c Reagent kit

5. Device Description

Instrument read, single use *in-vitro* test for quantitative determination of glycated hemoglobin in human whole blood.

6. Intended Use

Afinion™ AS100 Analyzer System, consisting of the Afinion™ AS100 Analyzer Afinion™ Test Cartridges and Afinion™ Controls is for *in-vitro* diagnostic use only. Afinion™ AS100 Analyzer is a compact multi-assay analyzer for point-of –care testing, designed to analyze the Afinion™ Test Cartridges. The Afinion™ Analyzer System is easy to use, rapid and gives reliable and accurate results.

Afinion™ HbA1c is an *in-vitro* test for quantitative determination of glycated hemoglobin in human blood. The measurement of % HbA1c is recommended as a marker of long-term metabolic control in persons with diabetes mellitus.

Afinion™ HbA1c Controls have been designed for use with the Afinion™ AS100 Analyzer System. Quality control using the Afinion™ HbA1c Control should be done to confirm that the Afinion™ AS100 Analyzer System is working properly and provides reliable results.

7. Summary of Safety and Effectiveness Information Supporting a Substantially Equivalent Determination

The formation of glycohemoglobins is principally a function of the concentration of glucose to which the erythrocytes are exposed. Glycated hemoglobin is a clinically useful index of mean glycemia during the preceding 6-8 weeks. Chronic elevated blood sugar level of persons with diabetes mellitus will over time cause damage to the small vessels of the body. The damages develop slowly over years and are known to cause late complications. Depending on the assay method, HbA1c is approximately 3-6 % in non-diabetics, 6-8 % in controlled diabetics and can be as much as 18 % or higher in poorly controlled diabetics.

The Afinion™ HbA1c is a fully automated assay for the determination of the percentage of HbA1c in human whole blood, by use of Afinion™ AS100 Analyzer.

Afinion™ AS100 Analyzer utilizes a digital camera and Light Emitting Diodes to perform two kinds of measurements; reflection measurement (amount of light reflected from a membrane) and transmission measurement (amount of light propagating through a liquid). The analyzer is self-calibrated and no calibration by user is needed.

Several fail-safe functions are provided to ensure the quality of assay results, to ensure that no erroneous results are presented to the user and to prevent mechanical damage to the analyzer itself. If an error should occur, an information code described in the User Manual is displayed.

Verification of the Afinion™ AS100 Analyzer has been performed and the results demonstrate compliance with specifications.

The results from the Afinion™ HbA1c assay are traceable to the International Federation of Clinical Chemistry (IFCC) Reference Method for measurement of HbA1c in human blood. NGSP (National Glycohemoglobin Standardization Program, US) recommends that HbA1c values are reported at DCCT-level (Diabetes Control and Complications Trial, US). The IFCC Working Group on Standardization of HbA1c has established a Master Equation for the Designated Comparison Method (the method used in the DCCT study, referred to as the NGSP Master Equation by the Working Group). This master equation (NGSP = 0.9148 IFCC + 2.152) is implemented in the Afinion™ AS100 Analyzer software and the Analyzer displays values at DCCT level.

The substantial equivalence, safety and efficacy of the Axis-Shield PoC Afinion™ HbA1c assay to Bayer DCA 2000® Hemoglobin A1c assay (K951361), 510(k) cleared 05/05/1995, CLIA Waived 11/12/1997, was evaluated internally and externally at three study sites.

Forty (40) venous EDTA blood samples were analyzed internally on both Afinion™ AS100 Analyzer and Bayer DCA 2000®. The Bland-Altman method comparison showed acceptable agreement with a bias of -0.3 % HbA1c and 95 % limit of agreement from -1.0 to 0.4 % HbA1c.

At three external study sites 75 venous EDTA blood samples were analyzed on both Afinion™ AS100 Analyzer and Bayer DCA 2000®. The linear regression comparison method showed acceptable agreement with; slope = 0.91, y-intercept = 0.2 % HbA1c and $r^2 = 0.96$.

39 venous EDTA blood samples from the European Reference Laboratory for glycohemoglobin (ERL) were analyzed internally by the Afinion™ HbA1c assay and by ERL with their reference method Primus CLC385. The Bland-Altman method comparison showed excellent agreement with a bias of 0.0 % HbA1c and 95 % limit of agreement from -0.3 to 0.3 % HbA1c.

Capillary and venous blood samples from 74 donors were analyzed externally with the Afinion™ HbA1c assay. The Bland-Altman comparison showed excellent agreement with a bias of 0.0 % and 95 % limit of agreement from -3.5 to 3.6 %. Linear regression; slope = 0.99, y-intercept = 0.1 % HbA1c and $r^2 = 0.99$.

Precision studies were performed according to Clinical and Laboratory Standards NCCLS guideline EP5-A by using two levels of blood samples (5.6 and 10.0 % HbA1c) and two Afinion™ HbA1c Controls (6.5 and 9.1 % HbA1c). The within-run CV was <1.0 % and the total CV was ≤1.4 % for both samples and controls.

The total precision of the Afinion™ HbA1c assay for two blood samples tested on ten Afinion™ AS100 Analyzers showed a CV of 2.1 % and 2.8 %, which is well within the acceptance criterion of CV ≤ 5 %.

Intended users at three external study sites performed external precision studies on three Afinion™ AS100 Analyzers. Two lots of Afinion™ HbA1c and three EDTA blood samples (A, B and C), analyzed for 10 operating days with six replicates of each sample, were used. The total precision showed a CV of < 2.5 % for all three EDTA samples.

Dilution linearity within the analytical range of 4-18 % HbA1c was demonstrated to meet all criteria for linearity. Dilution of high HbA1c sample by mixing with a sample with low HbA1c into seven intermediate concentrations showed a correlation coefficient $r^2 = 1.00$, slope = 1.01 and y-intercept = 0.07 % HbA1c.

Studies performed according to the ERL Manufacturer Check Up Certification procedure by ERL technical staff showed that the Hb-variants HbAC, HbAE, HbAD, HbAJ, HbAS, HbF and the derivate carbamylated Hb do not interfere with analyzes of % HbA1c on Afinion™ AS100 Analyzer.

Blood samples with up to 22 % preglycated hemoglobin (labile form) showed ≤ 5 % interference with the % HbA1c results when analyzed with the Afinion™ HbA1c assay.

Effect on quantification by endogenous interfering substances was tested. Bilirubin (0.2 mg/mL), glucose (5.0 mg/mL), lipids (triglycerides; 15.7 mmol/L and cholesterol; 9.1 mmol/L) or fructosamine (680 µmol/L) in EDTA blood samples gave ≤ 2 % interference when analyzed for % HbA1c on the Afinion™ AS100 Analyzer.

The possible interference from the prescription drugs glyburide and metformin and the over-the-counter (OTC) drugs acetaminophen, ibuprofen, acetylsalicylic acid and its active metabolite salicylic acid has been tested according to Clinical and Laboratory Standards NCCLS guideline EP7-A. Glyburide (3.9 µmol/L), metformin (310 µmol/L), acetaminophen (1.7 mmol/L), ibuprofen (1.8 mmol/L), acetylsalicylic acid (3.3 mmol/L) and salicylic acid (4.3 mmol/L) in EDTA blood samples gave ≤ 3 % interference when analyzed for % HbA1c on the Afinion™ AS100 Analyzer.

Hemolysed samples cannot be analyzed by the Afinion™ HbA1c assay. Samples with a degree of hemolysis above 6 % will result in information code 204 (*Hemolysed blood sample*) displayed on the Afinion™ AS100 Analyzer and no

result will occur. In samples with a low degree of hemolysis (below 6 %) a negligible interference (<4 %) was observed when analyzed with Afinion™ HbA1c.

Capillary samples and EDTA, Heparin, Na-citrate and NaF blood samples were collected from 10 donors. The results show no difference between the capillary and venous blood with different anticoagulants. The recoveries, compared to EDTA, varied between 98-103 % for each donor and anticoagulant. The average recoveries for each anticoagulant were 100-101 % compared to EDTA.

In total 51 error messages were observed during the external study period. All messages lead to an abortion of the assay followed by an ejection of cartridge. That no results were displayed in these cases shows that the fail-safe system is functioning satisfactory.
When considering the comparison studies between Afinion™ HbA1c and Bayer DCA 2000® Hemoglobin A1c and the additional documentation supporting the Afinion™ HbA1c, it can be concluded that the Axis-Shield PoC Afinion™ HbA1c when tested on the Afinion™ AS100 Analyzer is substantially equivalent to Bayer DCA 2000® Hemoglobin A1c assay (K951361).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
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JUL 2 2 2005

Axis- Shield PoC AS
c/o Ronald G. Leonardi, Ph.D.
President
R&R Registrations
P.O. Box 262069
San Diego, CA 92196-2069

Re: k050574
Trade/Device Name: Afinion™ HbA1c
Afinion™ HbA1c Controls
Afinion™ AS100 Analyzer
Regulation Number: 21 CFR 864.7470
Regulation Name: Glycosylated hemoglobin assay
Regulatory Class: Class II
Product Code: LCP, JJX, JQT
Dated: June 28, 2005
Received: July 5, 2005

Dear Dr. Leonardi:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Carol C. Benson

Carol C. Benson, M.A.
Acting Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K050574

Device Name: Afinion™ HbA1c, Afinion™ HbA1c Control and Afinion™ AS100 Analyzer

Indications For Use:

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(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

✓ Prescription Use (Per 21 CFR 801.109)

OR

Over-The-Counter Use (Optional Format 1-2-96)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K050574

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